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Novel disease associations with schizophrenia genetic risk revealed in ~400,000 UK Biobank participants

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ABSTRACT:

Schizophrenia is a serious mental disorder with considerable somatic and psychiatric morbidity. It is unclear whether comorbid health conditions predominantly arise due to shared genetic risk or consequent to having schizophrenia. To explore the contribution of genetic risk for schizophrenia, we analysed the effect of schizophrenia polygenic risk scores (PRS) on a broad range of health problems in 406,929 individuals with no schizophrenia diagnosis from UK Biobank. Diagnoses were derived from linked health data including primary care, hospital inpatient records, and registers with information on cancer and deaths. Schizophrenia PRS were generated and tested for associations with general health conditions, 16 ICD10 main chapters, and 603 diseases using linear and logistic regressions. Higher schizophrenia PRS was significantly associated with poorer overall health ratings, more hospital inpatient diagnoses, and more unique illnesses. It was also significantly positively associated with 4 ICD10 chapters: mental disorders; respiratory disease; digestive disease; and pregnancy, childbirth and the puerperium, but negatively associated with musculoskeletal disorders. Thirty-one specific phenotypes were significantly associated with schizophrenia PRS, and the 19 novel findings include several musculoskeletal diseases, respiratory diseases, digestive diseases, varicose veins, pituitary hyperfunction, and other peripheral nerve disorders. These findings extend knowledge of the pleiotropic effect of genetic risk for schizophrenia and offer insight into how some conditions often comorbid with schizophrenia arise. Further investigations examining the effect of potential mediating factors including smoking, alcohol consumption, and socioeconomic status may assist with future application of schizophrenia PRS in disease prediction or clinical practice.

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